REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the following remarks. With the above amendment, claims 62, 64-65, 67, and 69-70 have been canceled without prejudice. Claims 61, 63, 66, and 68, have been amended to more particularly point out one aspect of Applicants' invention and to remove dependency from canceled claims 61 and 67. It is urged that support for all the above amendments may be found throughout the specification as originally filed and that none of the amendments constitutes new matter. It should also be noted that the above amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application.

Rejection Under 35 U.S.C. § 112, first paragraph (written description)

Claims 61-70 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking written description. In particular, the Action asserts that the claims encompass a genus of various structural variants of the polypeptide sequence of SEQ ID NO:176 and includes numerous unknown and unidentified polypeptides that differ dramatically from the sequence of SEQ ID NO:176. The Action alleges that no common structural attributes identify the members of the genus. The Action further alleges that the phrase "wherein said polypeptide can be used for detection of lung cancer" in claim 61 and claims 62-64 dependent therefrom, is new matter. In particular, the Action contends that the specification fails to provide sufficient disclosure that any polypeptide can be used for the detection of lung cancer.

Applicants respectfully traverse this rejection on the following grounds.

Applicants submit that the claimed genus of polypeptides is more than adequately described in the specification as filed. In particular, Applicants describe that the claimed polypeptide of SEQ ID NO:176 has a lung-tumor expression profile. The PTO Guidelines on Written Description note that:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical

> and/or chemical functional characteristics when coupled with a known or disclosed correlation between function and structure of some combination of such characteristics. (Federal Register, Vol. 66, No. 4, June 5, 2001; page 1106, first column)

Applicants submit that a sufficient and relevant identifying characteristic shared by members of the currently claimed genus is the structural characteristic of having at least 75%-95% identity to SEQ ID NO:176. Applicants further submit that the skilled artisan would readily appreciate that Applicants' were indeed in possession of the claimed invention at the time of filing, in particular when this structural characteristic is combined with the functional characteristic shared by members of the currently claimed genus, *i.e.*, their ability to stimulate T cells that are specific for an amino acid sequence present in the polypeptide set forth in SEQ ID NO:176. These illustrative features of the claimed polypeptides are recited in the claims.

To accept the Action's position that Applicant was only in possession of an immunogenic composition comprising the specific species of SEQ ID NO:176 would thus inappropriately exclude an entire class of polypeptides related to SEQ ID NO:176 that the skilled individual would appreciate were in Applicants' possession at the time of filing. For example, given the Applicants' discovery that this polypeptide is expressed in lung tumor tissue relative to normal lung tissue, it is submitted that the skilled artisan would immediately recognize that the Applicants were in possession of much more than the specific sequence of SEQ ID NO:176. Rather, in view of this disclosure, and further in view of the level of general knowledge in this art, the skilled artisan would understand and expect that an entire class of polypeptides structurally related to SEQ ID NO:176, *e.g.*, sequences having at least 75%-90% identity to SEQ ID NO:176, would also be useful in the context of the Applicants' invention, despite the fact that they are not identical to the specific sequence of SEQ ID NO:176. The skilled artisan would indeed fully expect that such sequences related to SEQ ID NO:176 could be used, for example, in generating, *e.g.*, antibodies or T cells having specificity for a polypeptide sequence of SEQ ID NO:176, useful in the detection of lung cancer tissue, despite the fact that the sequences are not identical with the specific sequence of SEQ ID NO:176. This understanding and expectation on the part of the skilled artisan is submitted to be soundly based upon fundamental scientific principles.

Applicants submit that one skilled in the art would recognize, in light of the instant disclosure, an identifying characteristic shared by members of the claimed genus and that Applicant was in possession of this claimed genus at the time the application was filed.

With regard to the phrase "wherein said polypeptide can be used for detection of lung cancer" in claim 61 and claims 62-64 dependent therefrom, being new matter, Applicants respectfully direct the Examiner to page 107, line 24 through page 108, line 18 of the specification as filed where it is described that "...the above protocols may be readily modified to use the lung tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample." The specification goes on to state "A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a lung tumor protein in a biological sample." Accordingly, Applicants submit that the claimed subject matter is adequately described in the specification as filed and that the skilled artisan would readily appreciate in light of the instant disclosure, that polypeptides can be used for the detection of lung cancer, *e.g.* through the detection of reactive antibodies or T cells in a biological sample. Thus, Applicants respectfully submit that the above phrase does not constitute new matter.

Notwithstanding the aforementioned, without acquiescence and solely to expedite prosecution of one embodiment of the invention, Applicants have amended claim 61, without prejudice, to remove recitation of "wherein said polypeptide can be used for detection of lung cancer". Further, Applicants have amended claims 61 and 66 without prejudice to remove recitation of a polypeptide comprising an amino acid sequence having at least 75%-90% identity to SEQ ID NO:176.

Applicants urge that the claims satisfy the written description requirement under 35 U.S.C. § 112, first paragraph, and respectfully request reconsideration and withdrawal of the rejection.

Rejection Under 35 U.S.C. § 112, first paragraph (enablement)

Claims 61-64 are rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. Specifically, the Action alleges that, while the specification is enabling for a polypeptide comprising the amino acid sequence of SEQ ID NO:176, the specification is not

enabling for a polypeptide comprising an amino acid sequence having at least 75% or 90% identity to the sequence of SEQ ID NO:176. The Action further alleges that the specification fails to provide sufficient disclosure of the structural feature, such as an antigenic determinant, within the protein sequence of SEQ ID NO:176 that contributes to the production of antibodies specific to SEQ ID NO:176. The Action contends that the alteration of the amino acid sequence of a polypeptide can change its stereochemical shape or three dimensional conformation or its antigenic determinant region, and such alteration can change the ability of the polypeptide to produce antibodies specific for SEQ ID NO:176. The Action asserts that it would be unpredictable for one skilled in the art to determine which amino acid residue can be substituted, deleted, or added to SEQ ID NO:176 for the detection of lung cancer in a patient.

Applicants respectfully traverse the rejection and submit that the specification as filed fully enables the skilled artisan to make and use the invention. Applicants submit that one skilled in the art, using only routine methodologies described in the instant specification (*e.g.* Example 5) and/or available within the general level of knowledge in the art, and without undue experimentation, could readily determine whether the claimed polypeptides having at least 75%-95% identity to SEQ ID NO:176 could be used for the detection of lung cancer. For example, such a polypeptide could be used to generate antibodies and these antibodies could then be tested for their ability to detect L523S in lung cancer samples. However, solely to expedite prosecution, Applicants have amended claim 61 without prejudice, to remove recitation of a polypeptide comprising an amino acid sequence having at least 75%-90% identity to SEQ ID NO:176 or portions thereof.

Applicants respectfully submit that the above amendments and comments obviate and overcome the rejection. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 61-64 under 35 U.S.C. § 112, first paragraph.

Claims 65-70 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. Specifically, the Action alleges that claims 65-70 read on using the claimed immunogenic composition to stimulate T cells or an immune response in a patient so as to provide a therapeutic effect, such as inhibition of tumor growth or elimination of tumor cells, in said patient. Further, the Action contends that the specification fails to provide adequate guidance and evidence that the immunogenic composition comprising the claimed polypeptides

can stimulate any T cells or an immune response in a patient so as to provide a therapeutic effect, such as inhibition of tumor growth or elimination of tumor cells, in said patient. Additionally, the Action alleges that it would be unpredictable for one skilled in the art at the time of the invention to determine which amino acid residue can be substituted, deleted, or added to SEQ ID NO:176 such that the resulting polypeptide having at least 75%-90% identity to the sequence of SEQ ID NO:176 could still induce an immune response specific for various target tumor cells in a patient. Therefore, the Action concludes that one skilled in the art at the time of the invention would not know how to use the claimed polypeptides for the claimed invention.

As an initial matter, Applicants note that the claims do not recite using the composition to stimulate T cells in a patient so as to provide a therapeutic effect, such as inhibition of tumor growth or elimination of tumor cells, as alleged in the Action. Amended claims 65-70 comprise an independent composition claim (claim 66) and a composition claim dependent therefrom (claim 67). Claims 65 and 70 comprise claims directed to one method of using the compositions of the present invention, in particular for inducing an immune response in a patient. It appears from the Action's comments that in order to enable a composition it would be necessary to submit human clinical data. This is clearly not a requirement for patentability of a composition. In *In re Brana*, the Federal Circuit emphatically rejected the PTO position that human clinical testing is necessary to establish practical utility for an antitumor agent. 51 F.3d 1560.

As shown in the specification as filed, and noted on page 8 of the instant Action, since the polypeptide sequence of SEQ ID NO:176 is overexpressed in lung cancer as compared to normal lung tissue, it is considered a lung tumor protein. Applicants urge, as noted in the response filed July 5, 2002, that one skilled in the art, using only routine methodologies described in the instant specification (*e.g.* Example 5) and/or available within the general level of knowledge in the art, and without undue experimentation, could readily determine whether the claimed polypeptides having 75%-95% identity to SEQ ID NO:176 could be used, for example, for the detection of lung cancer. For example, such a polypeptide could be used to generate antibodies and these antibodies could then be tested for their ability to detect L523S in lung cancer samples. Applicants further submit that one skilled in the art, using only routine methodologies described in the instant specification and/or available within the general level of

knowledge in the art, and without undue experimentation, could readily determine whether the claimed polypeptides having 75%-95% identity to SEQ ID NO:176 stimulate T cells that are specific for the polypeptide of SEQ ID NO:176 (see for example, page 81, line 16 through page 83, line 4). Additionally, for example, the specification as filed clearly enables the particular method of using overlapping peptides to screen for T cell reactivity (see Example 7, page 133).

Notwithstanding the above, and solely to expedite prosecution of certain aspects of the present invention, Applicants have amended the claims without prejudice to remove recitation of amino acid sequences having at least 75%-95% identity to SEQ ID NO:176.

With regard to the method claims, Applicants do not acquiesce to the former grounds of rejection, however, Applicants have canceled claims 65 and 70 and wish to defer these points to a later filed continuation application in which the claims in their original scope will be prosecuted. Thus, Applicants urge that the pending claims fully satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph, and that the rejection of the claims under 35 U.S.C. § 112, first paragraph, may be properly withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 61, 62, 65-67 and 70 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Carney (US Patent No. 6,200,764) in view of Mueller-Pillasch *et al.* (*Oncogene 14*:2729-2733, 1997). In particular, the Action asserts that Carney teaches using carrier proteins and complete Freunds adjuvant to enhance immunogenicity of the Ras tumor protein. The Action states that Carney does not teach the polypeptide sequence of SEQ ID NO:176 or a polypeptide that is at least 75%-90% identical to SEQ ID NO:176. However, the Action asserts that Mueller-Pillasch *et al.* teaches a polypeptide identical to SEQ ID NO:176 that is overexpressed in pancreatic cancer cell lines and pancreatic cancer tissue as compared to normal pancreas. Therefore, the Action alleges that it would have been obvious for one of ordinary skill at the time of the invention to substitute Ras polypeptides with the human KOC polypeptide taught by Mueller-Pillasch to produce polyclonal antibodies. The Action contends that the skilled artisan would have been motivated to do so in order to produce antibodies specific for KOC more efficiently by using an immunostimulant such as an adjuvant, as taught by Carney. Further, the Action contends that since the human KOC transcript is highly

overexpressed in pancreatic cancer cell lines and pancreatic cancer tissue, the skilled artisan would have been motivated to use the human KOC polypeptide to generate KOC-specific antibodies in order to detect expression of KOC.

Applicants respectfully traverse this rejection and submit that the combined primary and secondary references, taken for what they teach as a whole, do not teach or suggest the claimed invention. Therefore, Applicants submit that the claimed invention would not have been obvious to the ordinarily skilled artisan at the time of filing.

Carney teaches using carrier proteins and complete Freunds adjuvant to enhance immunogenicity of Ras peptides for the express purpose of generating antibodies. Nowhere does Carney teach or suggest the polypeptide set forth in SEQ ID NO:176 nor does the cited reference teach or suggest an adjuvant that induces predominantly Th1-type responses as recited in the claims as amended. Mueller-Pillasch *et al.* does not overcome the deficiency of Carney. While Mueller-Pillasch *et al.* teaches the polypeptide of SEQ ID NO:176, nowhere does Mueller-Pillasch *et al.* teach or suggest combining the polypeptide of SEQ ID NO:176 with an adjuvant that induces predominantly a Th1-type response.

Moreover, even assuming *arguendo* that the cited references show elements of the Applicants' invention, there is no motivation for a skilled artisan to combine the cited references in order to arrive at the Applicants' claimed invention. The Federal Circuit has held that "when a rejection depends on a combination of prior art references, there must be some teaching, suggestion, or motivation to combine the references." *In re Rouffet*, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453, 1456 (Fed. Cir. 1998). As the Federal Circuit has reiterated, "virtually all inventions are combinations of old elements." Further, the Court noted that although an Examiner may often find every element of a claimed invention in the prior art, such a finding is insufficient to support a *prima facie* case of obviousness. To properly support a *prima facie* case of obviousness, the Examiner must show a motivation to combine the references. To this end, the Examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed. *In re Rouffet,* 47 USPQ2d 1453, 1458 (Fed. Cir. 1998) Further, when an Examiner relies on the skill in the art, the Examiner must "explain what specific understanding or technological principle within the knowledge of

one of ordinary skill in the art would have suggested the combination." *Id.* As noted by the Federal Circuit, if merely "a rote invocation [of the skill in the art] could suffice to supply motivation to combine, the more sophisticated scientific fields would rarely, if ever, experience a patentable technical advance." *Id.*

Without motivation to combine the prior art references, a skilled artisan would select and combine elements from the prior art only by examining the problem in hindsight. The Federal Circuit has firmly rejected such hindsight reconstruction used to "pick and choose among isolated disclosures in the prior art" to arrive at the Applicants' invention. *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988).

In view of the above comments, Applicants respectfully submit that the instant claims are not obvious in view of the cited references. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103(a).

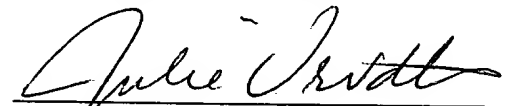
The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants respectfully submit that the claims remaining in the application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Tongtong Wang et al.

SEED Intellectual Property Law Group PLLC



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